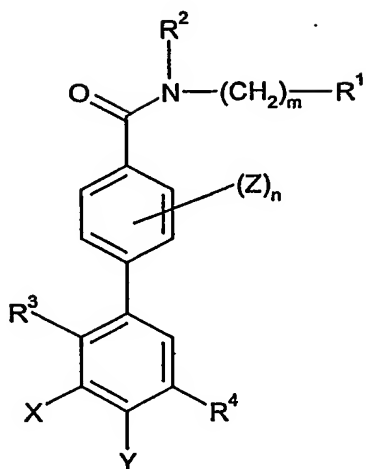


## CLAIMS

1. A compound of formula (I):



(I)

wherein

$R^1$  is selected from hydrogen,  $C_{1-6}$ alkyl optionally substituted by up to three groups independently selected from  $C_{1-6}$ alkoxy, halogen and hydroxy,  $C_{2-6}$ alkenyl,  $C_{3-7}$ cycloalkyl optionally substituted by one or more  $C_{1-6}$ alkyl groups, phenyl optionally substituted by up to three groups independently selected from  $R^5$  and  $R^6$ , and heteroaryl optionally substituted by up to three groups independently selected from  $R^5$  and  $R^6$ ,

$R^2$  is selected from hydrogen,  $C_{1-6}$ alkyl and  $-(CH_2)_p-C_{3-7}$ cycloalkyl optionally substituted by one or more  $C_{1-6}$ alkyl groups,

or  $(CH_2)_mR^1$  and  $R^2$ , together with the nitrogen atom to which they are bound, form a four- to six-membered heterocyclic ring optionally substituted by up to three  $C_{1-6}$ alkyl groups;

$R^3$  is chloro or methyl;

$R^4$  is the group  $-NH-CO-R^7$  or  $-CO-NH-(CH_2)_p-R^8$ ;

$R^5$  is selected from  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy,  $-(CH_2)_p-C_{3-7}$ cycloalkyl optionally substituted by one or more  $C_{1-6}$ alkyl groups,  $-CONR^9R^{10}$ ,  $-NHCOR^{10}$ ,  $-SO_2NHR^9$ ,  $-(CH_2)_qNHSO_2R^{10}$ , halogen, CN, OH,  $-(CH_2)_qNR^{11}R^{12}$ , and trifluoromethyl;

$R^6$  is selected from  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy, halogen, trifluoromethyl and  $-(CH_2)_qNR^{11}R^{12}$ ;

$R^7$  is selected from hydrogen,  $C_{1-6}$ alkyl,  $-(CH_2)_p-C_{3-7}$ cycloalkyl optionally substituted by one or more  $C_{1-6}$ alkyl groups, trifluoromethyl,  $-(CH_2)_p$ heteroaryl optionally substituted by  $R^{13}$  and/or  $R^{14}$ , and  $-(CH_2)_p$ phenyl optionally substituted by  $R^{13}$  and/or  $R^{14}$ ;

$R^8$  is selected from hydrogen,  $C_{1-6}$ alkyl,  $C_{3-7}$ cycloalkyl optionally substituted by one or more  $C_{1-6}$ alkyl groups,  $CONHR^9$ , phenyl optionally substituted by  $R^{13}$  and/or  $R^{14}$ , and heteroaryl optionally substituted by  $R^{13}$  and/or  $R^{14}$ ;

R<sup>9</sup> and R<sup>10</sup> are each independently selected from hydrogen and C<sub>1-6</sub>alkyl, or

R<sup>9</sup> and R<sup>10</sup>, together with the nitrogen atom to which they are bound, form a five- to six-membered heterocyclic ring optionally containing one additional heteroatom selected from oxygen, sulfur and N-R<sup>15</sup>, wherein the ring is optionally substituted by up to

5 two C<sub>1-6</sub>alkyl groups;

R<sup>11</sup> is selected from hydrogen, C<sub>1-6</sub>alkyl and -(CH<sub>2</sub>)<sub>p</sub>-C<sub>3-7</sub>cycloalkyl optionally substituted by one or more C<sub>1-6</sub>alkyl groups,

R<sup>12</sup> is selected from hydrogen and C<sub>1-6</sub>alkyl, or

10 R<sup>11</sup> and R<sup>12</sup>, together with the nitrogen atom to which they are bound, form a five or six-membered heterocyclic ring optionally containing one additional heteroatom selected from oxygen, sulfur and N-R<sup>15</sup>;

R<sup>13</sup> is selected from C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkoxy, -(CH<sub>2</sub>)<sub>p</sub>-C<sub>3-7</sub>cycloalkyl optionally substituted by one or more C<sub>1-6</sub>alkyl groups, -CONR<sup>9</sup>R<sup>10</sup>, -NHCOR<sup>10</sup>, halogen, CN, -(CH<sub>2</sub>)<sub>q</sub>NR<sup>11</sup>R<sup>12</sup>, trifluoromethyl, phenyl optionally substituted by one or more R<sup>14</sup>

15 groups and heteroaryl optionally substituted by one or more R<sup>14</sup> groups;

R<sup>14</sup> is selected from C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkoxy, halogen, trifluoromethyl and -NR<sup>11</sup>R<sup>12</sup>;

R<sup>15</sup> is selected from hydrogen and methyl;

X and Y are each independently selected from hydrogen, methyl and halogen;

20 Z is selected from -(CH<sub>2</sub>)<sub>s</sub>OR<sup>16</sup>, -(CH<sub>2</sub>)<sub>s</sub>NR<sup>16</sup>R<sup>17</sup>, -(CH<sub>2</sub>)<sub>s</sub>CH<sub>2</sub>CH<sub>2</sub>R<sup>16</sup>, -(CH<sub>2</sub>)<sub>s</sub>COOR<sup>16</sup>, -(CH<sub>2</sub>)<sub>s</sub>CONR<sup>16</sup>R<sup>17</sup>, -(CH<sub>2</sub>)<sub>s</sub>NHCOR<sup>16</sup>, -(CH<sub>2</sub>)<sub>s</sub>NHCONR<sup>16</sup>R<sup>17</sup>, -(CH<sub>2</sub>)<sub>s</sub>SO<sub>2</sub>R<sup>16</sup>, -(CH<sub>2</sub>)<sub>s</sub>SO<sub>2</sub>NR<sup>16</sup>R<sup>17</sup> and -(CH<sub>2</sub>)<sub>s</sub>NHSO<sub>2</sub>R<sup>16</sup>;

R<sup>16</sup> is selected from hydrogen, C<sub>1-6</sub>alkyl optionally substituted by up to two hydroxy groups, -(CH<sub>2</sub>)<sub>t</sub>OR<sup>18</sup>, -(CH<sub>2</sub>)<sub>t</sub>NR<sup>18</sup>R<sup>19</sup>, -(CH<sub>2</sub>)<sub>t</sub>NHSO<sub>2</sub>R<sup>18</sup>, -(CH<sub>2</sub>)<sub>t</sub>CONR<sup>18</sup>R<sup>19</sup>, -(CH<sub>2</sub>)<sub>t</sub>COOR<sup>18</sup>, -(CH<sub>2</sub>)<sub>t</sub>heteroaryl optionally substituted by up to

25 two groups independently selected from halogen, C<sub>1-6</sub>alkyl and oxo, and -(CH<sub>2</sub>)<sub>t</sub>phenyl optionally substituted by up to two groups independently selected from halogen, C<sub>1-6</sub>alkyl and C<sub>1-6</sub>alkoxy,

R<sup>17</sup> is selected from hydrogen and C<sub>1-6</sub>alkyl, or

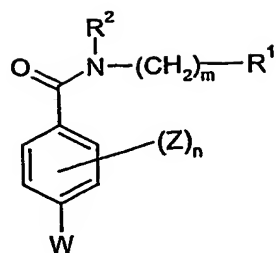
30 R<sup>16</sup> and R<sup>17</sup>, together with the nitrogen atom to which they are bound, form a five- to six-membered heterocyclic ring optionally containing one additional heteroatom selected from oxygen, sulfur and N-R<sup>15</sup>, wherein the ring is optionally substituted by up to two groups independently selected from oxo, halogen and C<sub>1-6</sub>alkyl;

R<sup>18</sup> and R<sup>19</sup> are each independently selected from hydrogen and C<sub>1-6</sub>alkyl optionally substituted by up to two hydroxy groups, or

35 R<sup>18</sup> and R<sup>19</sup>, together with the nitrogen atom to which they are bound, form a five- to six-membered heterocyclic ring optionally containing one additional heteroatom selected from oxygen, sulfur and N-R<sup>15</sup>, wherein the ring is optionally substituted by up to two groups independently selected from oxo, halogen and C<sub>1-6</sub>alkyl;

40 m is selected from 0, 1, 2, 3 and 4, wherein each carbon atom of the resulting carbon chain may be optionally substituted with up to two groups independently selected from C<sub>1-6</sub>alkyl and halogen;

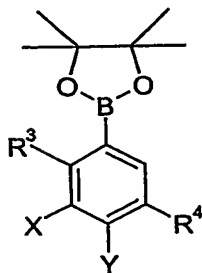
- n is 1;  
p is selected from 0, 1 and 2;  
q is selected from 0, 1, 2 and 3;  
r is selected from 0 and 1;  
5 s is selected from 0, 1, 2, 3 and 4; and  
t is selected from 1, 2, 3 and 4;  
or a pharmaceutically acceptable derivative thereof.
2. A compound according to claim 1 wherein R<sup>1</sup> is selected from C<sub>1-6</sub>alkyl, C<sub>3-7</sub>cycloalkyl and phenyl optionally substituted by up to three groups selected from R<sup>5</sup> and R<sup>6</sup>.  
10
3. A compound according to claim 1 or claim 2 wherein R<sup>1</sup> is C<sub>3-6</sub>cycloalkyl.
4. A compound according to any one of the preceding claims wherein R<sup>2</sup> is hydrogen.  
15
5. A compound according to any one of the preceding claims wherein m is 0 or 1.
6. A compound according to any one of the preceding claims wherein m is 1.  
20
7. A compound according to any one of the preceding claims wherein R<sup>8</sup> is C<sub>3-6</sub>cycloalkyl.
8. A compound according to any one of the preceding claims wherein Z is selected from -(CH<sub>2</sub>)<sub>s</sub>OR<sup>16</sup>, -(CH<sub>2</sub>)<sub>s</sub>NR<sup>16</sup>R<sup>17</sup>, -(CH<sub>2</sub>)<sub>s</sub>NHCOR<sup>16</sup>, -(CH<sub>2</sub>)<sub>s</sub>NHCONR<sup>16</sup>R<sup>17</sup> and -(CH<sub>2</sub>)<sub>s</sub>NHSO<sub>2</sub>R<sup>16</sup>.  
25
9. A compound according to claim 1 substantially as hereinbefore defined with reference to any one of Examples 1 to 48, or a pharmaceutically acceptable derivative thereof.  
30
10. A process for preparing a compound according to any one of claims 1 to 9, or a pharmaceutically acceptable derivative thereof, which comprises:  
35
- (a) reacting a compound of (II)



(II)

in which R<sup>1</sup>, R<sup>2</sup>, Z, m and n are as defined in claim 1 and W is halogen,  
with a compound of formula (III)

5

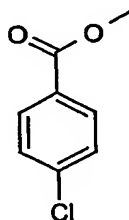


(III)

in which R<sup>3</sup>, R<sup>4</sup>, X and Y are as defined in claim 1,  
in the presence of a catalyst, or

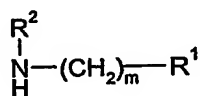
10

(b) reacting a compound of formula (VIII)



(VIII)

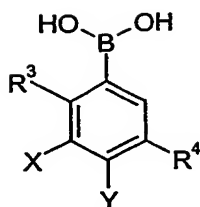
15 with a compound of formula (III) as hereinbefore defined and then reacting the acid thus  
formed with an amine of formula (V)



(V)

20 in which R<sup>1</sup>, R<sup>2</sup> and m are as defined in claim 1,  
under amide forming conditions

(c) reacting a compound of formula (II) as hereinbefore defined with a compound of  
formula (IX)

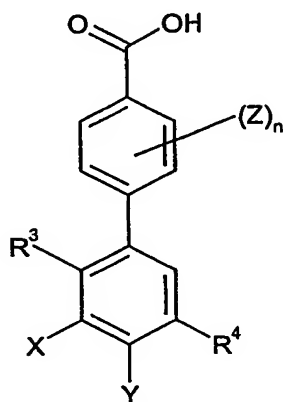


(IX)

in which  $R^3$ ,  $R^4$ , X and Y are as defined in claim 1,  
in the presence of a catalyst,

5

(d) reacting a compound of formula (X)

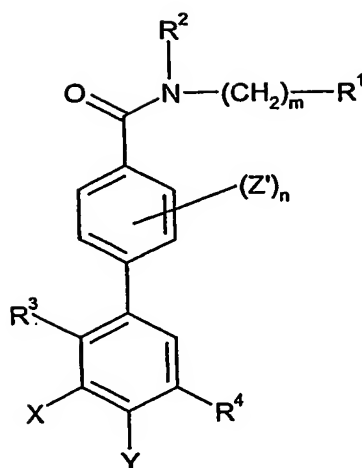


(X)

10 in which  $R^3$ ,  $R^4$ , X, Y, Z and n are as defined in claim 1,  
with an amine compound of formula (V) as defined above,  
under amide forming conditions,

) (e) final stage modification of one compound of formula (I) into another compound of  
15 formula (I), or

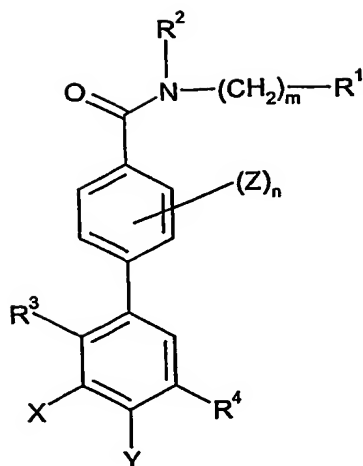
(f) conversion of a compound of formula (XII)



(XII)

in which Z' is a group convertible to Z as defined in claim 1.

- 5 11. A pharmaceutical composition comprising at least one compound according to any one of claims 1 to 9, or a pharmaceutically derivative thereof, in association with one or more pharmaceutically acceptable excipients, diluents and/or carriers
- 10 12. A method for treating a condition or disease state mediated by p38 kinase activity or mediated by cytokines produced by the activity of p38 kinase comprising administering to a patient in need thereof a compound according to any one of claims 1 to 9, or a pharmaceutically acceptable derivative thereof.
- 15 13. A compound according to any one of claims 1 to 9, or a pharmaceutically acceptable derivative thereof, for use in therapy.
- 20 14. Use of a compound according to any one of claims 1 to 9, or a pharmaceutically acceptable derivative thereof, in the manufacture of a medicament for use in the treatment of a condition or disease state mediated by p38 kinase activity or mediated by cytokines produced by the activity of p38 kinase.
15. A compound of formula (IA):



(IA)

wherein

$R^1$  is selected from hydrogen, C<sub>1-6</sub>alkyl optionally substituted by up to three groups independently selected from C<sub>1-6</sub>alkoxy, halogen and hydroxy, C<sub>2-6</sub>alkenyl, C<sub>3-7</sub>cycloalkyl optionally substituted by one or more C<sub>1-6</sub>alkyl groups, phenyl optionally substituted by up to three groups independently selected from  $R^5$  and  $R^6$ , and heteroaryl optionally substituted by up to three groups independently selected from  $R^5$  and  $R^6$ ,

$R^2$  is selected from hydrogen, C<sub>1-6</sub>alkyl and  $-(CH_2)_p$ -C<sub>3-7</sub>cycloalkyl optionally substituted by one or more C<sub>1-6</sub>alkyl groups,  
or  $(CH_2)_m R^1$  and  $R^2$ , together with the nitrogen atom to which they are bound, form a four- to six-membered heterocyclic ring optionally substituted by up to three C<sub>1-6</sub>alkyl groups;

$R^3$  is chloro or methyl;

$R^4$  is the group  $-NH-CO-R^7$  or  $-CO-NH-(CH_2)_p-R^8$ ;

$R^5$  is selected from C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkoxy,  $-(CH_2)_p$ -C<sub>3-7</sub>cycloalkyl optionally substituted by one or more C<sub>1-6</sub>alkyl groups,  $-CONR^9R^{10}$ ,  $-NHCOR^{10}$ ,  $-SO_2NHR^9$ ,  $-(CH_2)_qNHSO_2R^{10}$ , halogen, CN, OH,  $-(CH_2)_qNR^{11}R^{12}$ , and trifluoromethyl;

$R^6$  is selected from C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkoxy, halogen, trifluoromethyl and  $-(CH_2)_qNR^{11}R^{12}$ ;

$R^7$  is selected from hydrogen, C<sub>1-6</sub>alkyl,  $-(CH_2)_p$ -C<sub>3-7</sub>cycloalkyl optionally substituted by one or more C<sub>1-6</sub>alkyl groups, trifluoromethyl,  $-(CH_2)_r$ heteroaryl optionally substituted by  $R^{13}$  and/or  $R^{14}$ , and  $-(CH_2)_r$ phenyl optionally substituted by  $R^{13}$  and/or  $R^{14}$ ;

$R^8$  is selected from hydrogen, C<sub>1-6</sub>alkyl, C<sub>3-7</sub>cycloalkyl optionally substituted by one or more C<sub>1-6</sub>alkyl groups,  $CONHR^9$ , phenyl optionally substituted by  $R^{13}$  and/or  $R^{14}$ , and heteroaryl optionally substituted by  $R^{13}$  and/or  $R^{14}$ ;

$R^9$  and  $R^{10}$  are each independently selected from hydrogen and C<sub>1-6</sub>alkyl, or

$R^9$  and  $R^{10}$ , together with the nitrogen atom to which they are bound, form a five- to six-membered heterocyclic ring optionally containing one additional heteroatom

selected from oxygen, sulfur and N-R<sup>15</sup>, wherein the ring is optionally substituted by up to two C<sub>1-6</sub>alkyl groups;

R<sup>11</sup> is selected from hydrogen, C<sub>1-6</sub>alkyl and -(CH<sub>2</sub>)<sub>p</sub>-C<sub>3-7</sub>cycloalkyl optionally substituted by one or more C<sub>1-6</sub>alkyl groups,

5 R<sup>12</sup> is selected from hydrogen and C<sub>1-6</sub>alkyl, or

R<sup>11</sup> and R<sup>12</sup>, together with the nitrogen atom to which they are bound, form a five or six-membered heterocyclic ring optionally containing one additional heteroatom selected from oxygen, sulfur and N-R<sup>15</sup>;

10 R<sup>13</sup> is selected from C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkoxy, -(CH<sub>2</sub>)<sub>p</sub>-C<sub>3-7</sub>cycloalkyl optionally substituted by one or more C<sub>1-6</sub>alkyl groups, -CONR<sup>9</sup>R<sup>10</sup>, -NHCOR<sup>10</sup>, halogen, CN, -(CH<sub>2</sub>)<sub>q</sub>NR<sup>11</sup>R<sup>12</sup>, trifluoromethyl, phenyl optionally substituted by one or more R<sup>14</sup> groups and heteroaryl optionally substituted by one or more R<sup>14</sup> groups;

R<sup>14</sup> is selected from C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkoxy, halogen, trifluoromethyl and -NR<sup>11</sup>R<sup>12</sup>;

15 R<sup>15</sup> is selected from hydrogen and methyl;

X and Y are each independently selected from hydrogen, methyl and halogen;

Z is selected from -(CH<sub>2</sub>)<sub>s</sub>OR<sup>16</sup>, -(CH<sub>2</sub>)<sub>s</sub>NR<sup>16</sup>R<sup>17</sup>, -(CH<sub>2</sub>)<sub>s</sub>CH<sub>2</sub>CH<sub>2</sub>R<sup>16</sup>, -(CH<sub>2</sub>)<sub>s</sub>COOR<sup>16</sup>, -(CH<sub>2</sub>)<sub>s</sub>CONR<sup>16</sup>R<sup>17</sup>, -(CH<sub>2</sub>)<sub>s</sub>NHCOR<sup>16</sup>, -(CH<sub>2</sub>)<sub>s</sub>NHCONR<sup>16</sup>R<sup>17</sup>, -(CH<sub>2</sub>)<sub>s</sub>SO<sub>2</sub>R<sup>16</sup>, -(CH<sub>2</sub>)<sub>s</sub>SO<sub>2</sub>NR<sup>16</sup>R<sup>17</sup> and -(CH<sub>2</sub>)<sub>s</sub>NHSO<sub>2</sub>R<sup>16</sup>;

20 R<sup>16</sup> is selected from hydrogen, C<sub>1-6</sub>alkyl, -(CH<sub>2</sub>)<sub>t</sub>OR<sup>18</sup>, -(CH<sub>2</sub>)<sub>t</sub>NR<sup>18</sup>R<sup>19</sup>, -(CH<sub>2</sub>)<sub>t</sub>COOR<sup>18</sup>, -(CH<sub>2</sub>)<sub>t</sub>heteroaryl optionally substituted by up to two groups independently selected from halogen and C<sub>1-6</sub>alkyl, and -(CH<sub>2</sub>)<sub>t</sub>phenyl optionally substituted by up to two groups independently selected from halogen, C<sub>1-6</sub>alkyl and C<sub>1-6</sub>alkoxy,

25 R<sup>17</sup> is selected from hydrogen and C<sub>1-6</sub>alkyl, or

R<sup>16</sup> and R<sup>17</sup>, together with the nitrogen atom to which they are bound, form a five- to six-membered heterocyclic ring optionally containing one additional heteroatom selected from oxygen, sulfur and N-R<sup>15</sup>, wherein the ring is optionally substituted by up to two groups independently selected from oxo, halogen and C<sub>1-6</sub>alkyl;

30 R<sup>18</sup> and R<sup>19</sup> are each independently selected from hydrogen and C<sub>1-6</sub>alkyl, or

R<sup>18</sup> and R<sup>19</sup>, together with the nitrogen atom to which they are bound, form a five- to six-membered heterocyclic ring optionally containing one additional heteroatom selected from oxygen, sulfur and N-R<sup>15</sup>, wherein the ring is optionally substituted by up to two groups independently selected from oxo, halogen and C<sub>1-6</sub>alkyl;

35 m is selected from 0, 1, 2, 3 and 4, wherein each carbon atom of the resulting carbon chain may be optionally substituted with up to two groups independently selected from C<sub>1-6</sub>alkyl and halogen;

n is 1;

40 p is selected from 0, 1 and 2;

q is selected from 0, 1, 2 and 3;

r is selected from 0 and 1;



s is selected from 0, 1, 2, 3 and 4; and  
t is selected from 2, 3 and 4;  
or a pharmaceutically acceptable derivative thereof.